

REMARKS

Applicants note that claims 71 and 76-78 have been canceled. New claims 79-84 have been added to more distinctly claim the subject matter Applicants regard as their invention. As will be discussed below, the new claims are supported by the specification. No new matter has been added.

1. The Written Description Rejection

Claims 76-78 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was allegedly not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the invention at the time the application was filed. In particular, the Examiner asserts that although Applicants describe a structure having the atomic coordinates depicted in Appendix 1, the specification does not provide any disclosure for coordinates for amylases other than SEQ ID NO. 13, and therefore the Examiner concludes that the specification does not contain a written description sufficient to put one skilled in the art in possession of all of the species within the claimed genus of three dimensional structures of alpha-amylases.

In response, Applicants submitted an amendment dated February 28, 2001, attached hereto as Appendix A is a copy of the amendment. In response to the amendment submitted, an advisory action was issued. Furthermore, a personal interview was conducted on February 14, 2001. In the Interview Summary it was stated that the "Applicant has been advised that the claim[ed] method should consider a step of modeling a structure of a parent amylase on the crystal structure of SEQ ID NO:13 defined by the coordinates depicted in Appendix". A telephonic interview was conducted on March 19, 2001. The Interview Summary of that interview stated "The amendments should be made to items (a) and (b) in claims 79 and 80 to describe how the three dimensional structure was provided in (a) and how (by which method) "identifying" was carried out in (b)".

Applicants, in response to the issues raised in the two interviews and to further address the issues raised in the Office Action, have submitted new claims 79-84. It is specifically recited in the preambles of claims 79, 82 and 84 that the variant has an altered property relative to the parent alpha-amylase wherein said altered property is selected from the group consisting of substrate specificity, substrate binding, substrate cleavage pattern, temperature stability, pH dependence of enzymatic activity, pH dependence of stability, stability towards oxidation, Ca^{2+} -dependency and specific activity, where the parent alpha-amylase has a sequence of at least 70% homology to the sequence of SEQ ID No: 13, when homology is determined by the GAP program (Genetic Computer Group, Version 7.3) using default values for GAP penalties. Furthermore, step (a) of claim 79, it is recited that a three dimensional model of an alpha-amylase structure is generated utilizing data from Appendix 1 and a computer programmed for generating such a model from the data; step (a) of claim 82 recites that the model of a three dimensional alpha-amylase structure generated is defined by the atomic coordinates shown in Appendix 1 and step (a) of claim 84 recites that the model of a three dimensional structure of an alpha-amylase structure is generated using a computer programmed for generating a model structure and atomic coordinates shown in Appendix 1. Step (a) of claims 79, 82 and 84 are supported by Examples 1-3.

Applicants further point out that step (b) in new claims 79, 82 and 84 recites that mutations are identified using the model generated in step (a). Dependent claims 80 and 83 recite that step (a) further comprises using modeling methods and is supported by Example 3. Applicants further note that dependent claim 81 recite further characteristics of the alpha-amylase, specifically, that the three-dimensional alpha amylase structure has an A domain, a B domain and a C domain, wherein said A domain has an amino acid sequence corresponding to residues 1-103 and 206-305 of SEQ ID NO: 2; said B domain has an amino acid sequence corresponding to residues 104-205 of SEQ ID No. 2 and said C domain has an amino acid sequence corresponding to residues 396-483 of SEQ ID NO.2

Applicants assert that the new claims indeed meet the written description requirement. The Written description guidelines state with respect to a claim drawn to a genus:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

A sufficient number of identifying characteristics were certainly disclosed with respect to the variants obtained with respect to the method of the present invention. Applicants note that the atomic coordinates for the three-dimensional structure for SEQ ID NO. 13 as depicted in Appendix 1 are proposed by Applicants to be representative of all Termamyl-like alpha-amylases (see page 11, lines 20-22). Therefore, Applicants have also described the three-dimensional structure of other highly homologous alpha-amylases (70% homology to SEQ ID NO. 13), such as SEQ ID NOS. 2, 4, and 6. Furthermore, in the new claim 79, it is specifically recited that the alpha-amylase three dimensional model is generated utilizing the data from Appendix 1, in claim 82 it is recited that the three-dimensional model is defined by the atomic coordinates shown in Appendix 1 and in claim 84, it is recited that the alpha-amylase three dimensional model is generated using a computer programmed for generating a model structure and atomic coordinates shown in Appendix 1. In conclusion, the new claims meet the Written Description Requirement. Therefore, Applicants respectfully request that the rejection be withdrawn.

2. The Enablement Rejection

Claims 76-78 have been rejected under 35 U.S.C. 112, as lacking enablement. Specifically, the Examiner asserts that the specification is enabling only for a method of using a three-dimensional structure having coordinates depicted in Appendix 1. Furthermore, the Examiner asserts that given the unpredictability of X-ray

crystallography, one skilled in the art would need an X-ray crystallographic three-dimensional structure of an unspecified alpha-amylase.

Applicants respectfully disagree. One of ordinary skill in the art can readily provide an accurate three-dimensional structure of an enzyme once information about the three-dimensional structure of an enzyme with sufficient homology is known, for example, by alignment between the amino acid sequences of the enzymes of interest and/or by using various computer homology based modeling programs, such as INSIGHT, which was used in Example 1. Therefore, Applicants have provided an enabling disclosure for methods for obtaining variants with sufficiently high homology (70%) to SEQ ID NO. 13, such as SEQ ID NOS. 2, 4, and 6.

Furthermore, as noted above, in the new claim 79, it is specifically recited that the alpha-amylase three dimensional model is generated utilizing the data from Appendix 1, in claim 82 it is recited that the three-dimensional model is defined by the atomic coordinates shown in Appendix 1 and in claim 84, the three dimensional model is generated using alpha-amylase three dimensional model is generated using a computer programmed for generating a model structure and atomic coordinates shown in Appendix 1. The variants obtained using the methods claimed would have an altered property selected from the group consisting of substrate specificity, substrate binding, substrate cleavage pattern, temperature stability, pH dependence of enzymatic activity, pH dependence of stability, stability towards oxidation, Ca^{2+} -dependency and specific activity. An enabling disclosure is certainly disclosed for obtaining such variant by generating a three-dimensional model utilizing data from Appendix 1.

In view of new claims 79-84, Applicants assert that the rejections have been overcome. Therefore, Applicants respectfully request that the rejections be withdrawn.

3. The Indefiniteness Rejection

Claims 71 and 76-78 have been rejected under 35 U.S.C. 112 as indefinite for various reasons. It is respectfully submitted that the new claims render moot the indefiniteness rejection. Applicants respectfully request reconsideration and withdrawal of the rejection.

4. The Double Patenting Rejection

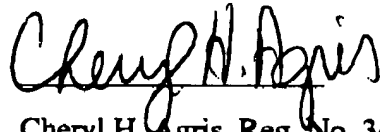
Claims 71 and 76-78 have been rejected under the judicially created doctrine of double patenting over claims 1-14 of U.S. Patent No. 5,989,169. In response, Applicants will address this issue upon indication of allowable subject matter.

5. Conclusions

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone at (914) 712-0093 if there are any questions concerning this amendment or application.

Respectfully submitted,

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